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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Francois Rousseau

Serial No.: Not Yet Assigned

Filing Date: March 15, 2001

For: MARKER AT THE ANDROGEN RECEPTOR GENE FOR DETERMINING BREAST CANCER SUSCEPTIBILITY

Examiner: Not Yet Assigned

Art Unit: Not Yet Assigned



**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

For entry to the United States national phase of International Application PCT/CA99/00852, please enter the following preliminary amendments to the claims:

## I. AMENDMENTS

In the claims:

6. (Amended) The method according to claim 1, wherein said polymorphism at the AR gene, or marker in linkage disequilibrium therewith, is determined from DNA obtained from said individual.

13. (Amended) The method of claim 1, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

15. (New) The method of claim 2, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

16. (New) The method of claim 6, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

17. (New) The method of claim 8, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

18. (New) The method of claim 12, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

## II. REMARKS

Attached on separate sheets is a clean copy of the claims as amended, as well as a marked-up copy of the amended claims.

Applicant believes that the above amendments place the application in condition for allowance. If a telephone call would further prosecution of this case, the Examiner is invited to call the undersigned attorney at (619) 234-6655.

In the unlikely event that the transmittal letter is separated from this document and/or the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-0872**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 15, 2001

Respectfully submitted,

By: _____

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Clean Copy of Amended Claims

1. A method of determining an individual's predisposition to breast cancer, development of breast cancer and/or responsiveness to therapy for breast cancer, said method comprising the step of determining a polymorphism at the CAG repeat of the androgen receptor (AR) gene or a DNA variant equivalent, or mutation which shows a linkage disequilibrium therewith, whereby said polymorphism at the AR gene, or marker in linkage disequilibrium therewith enables a prediction of an individual's predisposition to breast cancer, development of breast cancer and/or responsiveness to therapy for breast cancer.

2. The method of claim 1, wherein the androgen receptor genotype is determined by determining the number of CAG repeats within the androgen receptor gene

3. The method of claim 2, which further comprises a step of amplifying a segment of the androgen receptor using polymerase chain reaction.

4. The method of claim 3, wherein a pair of primers derived from a nucleic acid sequence of the androgen receptor gene or flanking said gene is used in the polymerase chain reaction.

5. The method of claim 4, wherein the segment of the androgen receptor gene is amplified using a pair of primers as follows:

| | |
|---|---|
| 5'-TCCAGAATCT GTTCCAGAGC GTGC-3' | SEQ ID NO:1; and |
| 5'-GCTGTGAAGG TTGCTGTTCC TCAT-3' | SEQ ID NO:2. |

6. (Amended) The method according to claim 1, wherein said polymorphism at the AR gene, or marker in linkage disequilibrium therewith, is determined from DNA obtained from said individual.

7. The method of claim 6, wherein said DNA is genomic DNA.

8. The method according to claim 7, wherein said DNA is obtained from non-cancerous cells.

9. The method of claim 8, wherein said cell is obtained from a tissue or blood sample.

10. An assay for screening and selecting an agent which modulates breast cancer predisposition comprising:

a) a recombinant androgen receptor (AR) gene or functional fragment thereof, which comprises a CAG repeat polymorphism in exon 1 thereof, or a marker in linkage disequilibrium therewith; and

b) assaying a function of said androgen receptor;

wherein an allele which modulates said function of said androgen receptor can be selected, and wherein a modulation of a function of said androgen receptor is associated with a modulation of said breast cancer predisposition, whereby short CAG repeats of said AR positively modulate androgen receptor function, while long CAG repeats of said AR negatively modulate Androgen receptor function, thereby leading to breast cancer protection or breast cancer predisposition.

11. An assay for screening and selecting an agent which modulates breast cancer predisposition comprising:

a) an expression vector comprising a promoter operably linked to a reporter gene, said promoter comprising an androgen response element, said response element affecting the activity of said promoter upon binding thereto of androgen or analog thereof;

b) a cell expressing a chosen allele of an androgen receptor and harboring said vector of a);

c) submitting said cell to at least one agent; and

d) assaying a level of said reporter gene;

whereby an agent which modulates breast cancer predisposition can be selected when the level of said reporter gene is significantly modulated by the presence of said agent through its action through the androgen receptor.

12. A method for screening and selecting an agent which can modulate breast cancer predisposition comprising:

a) selecting a specific allele of the androgen receptor (AR) gene, variant, equivalent, or mutation thereof which shows linkage disequilibrium therewith;

b) assaying a function of said AR allele of a); and

c) selecting an agent which can modulate breast cancer predisposition,

wherein an agent which modulates AR function is selected as an agent capable of modulating breast cancer predisposition when said function is significantly different in the presence of said agent, as compared to in the absence thereof.

13. (Amended) The method of claim 1, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

14. The method of claim 12, wherein said assay is a *cis-trans* assay.

15. (New) The method of claim 2, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

16. (New) The method of claim 6, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

17. (New) The method of claim 8, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.

18. (New) The method of claim 12, wherein the shortest alleles or a combination thereof are associated with a protection to breast cancer, and the intermediate to large alleles or a combination of the intermediate and largest alleles are associated with a predisposition to breast cancer.